

HIGH-THROUGHPUT AND MINIATURIZED RESIN REUSE STUDIES

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The major process limitations of current antibody purification processes are posed by affinity chromatography. Protein A-based chromatography can account for more than 70% of downstream processing costs due to resin throughput, cost and complexity of scale up.

A standard industrial practice to minimize resin cost has been to recycle its use over an extended period, aiming for >200 cycles. Results from a recent survey suggest that the number of Protein A cycles currently used for in the industry is much lower typically between 50–100 cycles (Rathore et al., 2015). Impurities that have not been removed may cause carryover from one cycle to the next, reducing the lifetime use of the resin, and therefore, effective cleaning of the resin becomes an important factor in reuse lifetime.

However, the screening of a large number of cleaning conditions may not be practical or economically feasible at laboratory scale due to the large amount of feedstream and resources required for each experiment (10-100 mL). To overcome this issue, techniques that can generate data with minimal resource expenditure by mimicking large scale processes can be invaluable. Typically, automating such studies at microscale poses great challenges due to the non-geometric scalability of the microscale columns with the lack of online UV monitoring.

In this presentation we will show how automated high throughput resin reuse studies performed on microscale columns can preempt potential issues with cleaning, feedstream, yield and chromatographic profile prior to scale up whilst requiring minimal human resources and material (20-2000 μ L). Data from screening 50 different cleaning solutions in single and in combination on 600 μ L microscale columns whilst using only 1.5% of laboratory scale feed material will be presented. Furthermore, a comparison to the performance of bench scale columns (4.7 mL) will be discussed.

Although automated high-throughput and miniaturized chromatographic process development relying on microscale columns is widespread, we believe this to be the first report of successful miniaturization of resin cleaning and reuse studies.

Rathore, A., Pathak, M., Ma, G., Bracewell, D., (2015) Re-use of protein A resin: fouling and economics. *Biopharm Int.* 3; 28